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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FLOOD, MICHELE C	
ART UNIT	**PAPER NUMBER**
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/420,092	Luo et al.
Examiner	**Art Unit**
Michele Flood	1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 9, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *15-17, 20, and 21* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *15-17, 20, and 21* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 27
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 26, 2003 has been entered.

Acknowledgment is made of the receipt and entry of the declaration filed under 37 CFR § 1.132 filed on April 2, 2003.

Acknowledgment is made of Applicant's cancellation of Claims 10-14.

Claims 15-17 and 20-21 are under examination.

Specification/Abstract

2. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the

printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc. In the instant case, the phrase "The present invention" and the term "novel" should be avoided.

3. Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves

modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:

(1) if a machine or apparatus, its organization and operation;

(2) if an article, its method of making;

(3) if a chemical compound, its identity and use;

(4) if a mixture, its ingredients;

(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

In the instant case, the content of the abstract is generally confusing and fails to describe the instantly claimed invention. For instance, the sentence that appears in lines 2-6 of the abstract is generally nonsensical: "Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the

present invention." A read of the abstract fails to apprise the reader the subject matter of the instantly claimed invention.

Appropriate correction is required.

The disclosure is objected to because of the following informalities:

On page 8, line 12, line 20, line 25, and line 30, Applicant recites "Figure" without disclosing the number of the figure to which Applicant refers.

Appropriate correction is required.

Response to Arguments

4. Applicant's arguments have been fully considered but they are not persuasive.

Full consideration was given to the declaration of Yasumichi Hitoshi, M.D., Ph.D. pursuant to 37 CFR § 1.132 filed on April 2, 2003. The declaration of Hitoshi is directed to the idea that the present invention does provide a "real world" use for the claimed invention. Hitoshi argues that R0101 is a cell cycle protein that has increased expression associated with certain cancers, and that one of skill in the art would recognize R0101 as a useful protein and that bioactive agents that bind thereto are also useful: "For example, one of skill in the art would expect that bioactive agents that bind to a protein known to be overexpressed in certain cancers,

as in R0101, would be useful as indicators of expression of the R0101 and therefore as a diagnostic or prognostic indicators of certain cancers." Hitoshi points to Figure 5, in an attempt, to support his position that proteins that are overexpressed in cancer cells can be used in diagnostic or prognostic evaluation of the disease. Hitoshi further argues that the specification provides ample evidence to conclude that PCNA protein (a protein with a recognized role in DNA synthesis) is a ligand for alleged cell cycle protein R0101, and points to Figure 6 to demonstrate the binding of R0101 to PCNA in cells. Next, Hitoshi argues that the specification enables the skilled practitioner to identify bioactive agents that bind to R0101, and asserts that methods to determine molecules that bind to a protein are known to those skilled in the art, as set forth in the present specification. Thus, Hitoshi concludes that "it is perfectly reasonable to expect the identification of bioactive agents that bind to R0101, a cell cycle protein that is highly expressed in some cancers, is an appropriate strategy to identify specific diagnostic or prognostic tools for certain cancers."

The Office respectfully disagrees, and does not find the arguments set forth by Hitoshi persuasive for the reasons set forth in the previous Office and for the reasons set forth below, under 35 USC § 101 and the first paragraph of 35 US § 112.

Claim Rejections - 35 USC § 101

Claims 15-17 and 20 as amended and newly added Claim 21 remain/are rejected under 35 U.S.C. § 101 because the claims are drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance. The rejection stands for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant's main argument is directed to the idea that the present specification characterizes the biological significance of protein R0101; and, thus, Applicant points to Figures 2B, and 4-8 to demonstrate the overexpression of R0101 in cancer tissue as compared to normal tissue, the location of R0101 in the nucleus, *etc.* However, Applicant's arguments are not persuasive because it is still clear from the instant specification that the protein described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966),

in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", " [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein of as yet undetermined function or biological significance. The claims are drawn to an isolated alleged cell cycle protein R0101 encoding Seq. ID No.: 2. The instant specification discloses that the claimed amino acid sequence can be employed to screen bioactive agents, when the cell cycle protein R0101 is combined with a bioactive agent by determining the binding capacity of the bioactive agent to the said alleged cell cycle protein R0101 (Seq. ID No.: 2). The specification discloses that such a screening assay can

be employed to identify compounds, which act as modulators of cell cycle activity. The instant application discloses that there are a plurality of different modulators that promote, enhance or deter inhibitors of cell proliferation and that the identification of such cell cycle components and modulators is highly desirable for the therapeutic use thereof. The instant specification further discloses that there are a plurality of different mammalian proteins which are known to function as alleged cell cycle proteins. However, neither the instant specification nor the art of record identifies even a single disease or disorder that has been shown to be associated with alleged cell cycle protein R0101, the claimed amino acid and the protein encoded thereby can not be employed in either a screening or diagnostic capacity. For example, the instant specification incorporates by reference the teachings of Nagase et al. (DNA Research, 1995, 2: 37-43) on page 2, lines 5-6, of the instant specification. However, there is absolutely no evidence of record or any line of reasoning that would support a conclusion that the protein of the instant invention is associated in any way with the plurality of causally unrelated cDNA sequences cited in the reference of Nagase et al. in Table 3. For instance, Applicant asserts that the instant R0101 (Seq. ID No.: 2) as a alleged cell cycle protein without providing any evidence or examples to support such a conclusion. Thus, Applicant's assertion appears to be purely speculative and wholly unsupported by any evidence of record. Since the prior art indicates a mere 14% amino acid sequence identity to a protein without an established function of the instantly claimed alleged cell

cycle protein R0101 encoding Seq. ID No.: 2, one of ordinary skill in the art would not reasonably extrapolate or conclude a common function between structurally dissimilar proteins, much less one having 95% amino acid sequence identity to the amino acid sequence set forth in Seq. ID No.: 2 as instantly claimed by Applicant. Neither the instant specification or the art of record identifies even a single disease or disorder that has been shown to be associated with alleged cell cycle protein R0101 of the instant invention. Since the alleged cell cycle protein R0101 of the instant invention has not been shown to be associated with a particular physiological process that an artisan would wish to manipulate for assaying bioactive agents for the identification of compounds which bind thereto, the claimed alleged cell cycle protein R0101 can not be used to identify compounds which would have the clinical effect of modulating processes of the cell cycle or which would be ultimately employed in a diagnostic capacity and therapeutic use thereof. Until some actual and specific significance can be attributed to the protein identified in the specification as alleged cell cycle protein R0101 (Seq. ID No.: 2), or the gene encoding it, the instant invention is incomplete. The protein encoded by a DNA of the instant invention is a compound known to be structurally analogous to proteins which are known in the art as alleged cell cycle proteins. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of bioactive agents capable of

binding to the said alleged cell cycle protein R0101 is clearly to use it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability.

While Applicant and the declaration of Hitoshi argue that the specification shows to one of ordinary skill in the art that R0101 is associated with certain cancers as set forth in Figure 5, the Office notes that there is nothing in the rendering of Figure 5 or the description of Figure 5 on page 4 of the specification, line 6, that would indicate the nexus between the overexpression of R010 alleged cell cycle protein in cancerous cell types and the use of R010 protein as a target to identify agents that bind thereto for either diagnostic or prognostic screening assays for cancer. For instance, it is unclear from any of the illustrated figures whether Applicant shows protein binding, nucleic acid or mRNA binding to any of the cell types. Moreover, it is unclear as to whether the overexpression of R010 in certain cancerous disease conditions is a protein marker indicative of cancer or whether the associated overexpression of the R010 protein is merely a result of an increase in metabolic protein activity. Although Applicant and Hitoshi both argue that the claimed screening method has utility for the routine identification of bioactive agents that bind to R010 protein, *i.e.*, for the diagnosis of, or prognostic evaluation of cancer, the Office maintains that since the instant specification does not disclose a credible "real world" use for

alleged cell cycle protein R0101 then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claims 15-17 and 20-21 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-17 and 20-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments have been fully considered but they are unpersuasive for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant speculates a method for screening for a bioactive agent capable of binding to the alleged cell cycle protein R0101, said method comprising: (a) combining a alleged cell cycle protein R0101 (Seq. ID No.: 2) and a candidate bioactive agent; and (b) determining the binding

of said candidate bioactive agent to said alleged cell cycle protein R0101; wherein said alleged cell cycle protein R0101 comprises an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in SEQ ID NO:2 and wherein said alleged cell cycle protein R0101 binds to proliferating cell nuclear antigen (PCNA). The claim is further directed to a method wherein said alleged cell cycle protein R0101 comprises the amino acid sequence set forth in SEQ ID NO:2; wherein the candidate bioactive agent is a member of a library of candidate bioactive agents and the cell is a member of a plurality of cells comprising a recombinant nucleic acid encoding R0101 protein; wherein binding modifies the activity of R0101 protein; and wherein step a) further comprises combining PCNA with alleged cell cycle protein R0101 and the candidate bioactive agent.

It appears that Applicant argues that since the claimed invention is supported by a specific, substantial, and credible utility and since the specification provides an activity for R0101 in binding to PCNA, and discloses an association between R0101 and specific cancers and provides methods of identifying bioactive agents that bind to R0101 and methods of using thereof, the Office should withdraw the rejection made under 35 USC, first paragraph. However, as set forth above, Applicant's assertion is not enabled because there is no way of determining whether the protein corresponding to (Seq. ID No.: 2) corresponds to any known protein with known activity, but for which the sequence is unknown. Therefore, the broad concept of using a alleged cell cycle protein with (Seq. ID No.: 2) in a screening assay for determining the binding of candidate bioactive agents to the alleged cell cycle protein R0101 is clearly beyond the skill of

one of ordinary skill in the art, requiring enormous burden and experimentation without a reasonable expectation of success. For example, with regard to Hitoshi's and Applicant's apparent argument that their is an association between overexpression of alleged cell cycle protein R0101 and cancer, the Office holds that overexpression of the mRNA protein could mean that it is a metabolically active protein, instead of being associated with a protein which is associated with or disease causing; and, thus it would be expected that the mRNA expression would be elevated. Because Applicant has not established a substantial and credible nexus between the overexpression of alleged cell cycle protein R0101 and the occurrence of cancerous cell types, it is unclear as how one would be able to determine the meaning for the binding of alleged cell cycle protein R0101 to any candidate bioactive agent. Speculation does not constitute enablement.

Claims 15-17 and 20-21 as amended are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks adequate written description for the claimed invention in view of the following points in accordance with the written description requirements of 35 U.S.C. 112:

The description must clearly allow persons of ordinary skill in the art to recognize what is claimed. Thus, an applicant must comply with the written description requirement "by describing

the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of the ingredients requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984). Accordingly, describing a method for screening for a bioactive agent capable of binding to a alleged cell cycle protein comprising combining the alleged cell cycle protein and a candidate bioactive agent generally known to exist, in the absence of knowledge as how to determine whether binding has occurred between the alleged cell cycle protein and the bioactive agent is not a description of the material or the method of use thereof. In the instant case and with regard to the arguments set forth in the declaration of Hitoshi, on page 23 of the specification, line 33 through page 27, line 26, Applicant describes candidate bioactive agents, and on page 27 of the specification, line 31 through page 31, line 32, Applicant discloses general embodiments of methods for screening for bioactive agents comprising combining a alleged cell cycle protein and a candidate bioactive agent, and evaluating the effect of the combining on cell cycle activity. However, the mere disclosure that those skilled in the art would know how to perform the instantly claimed invention for the determination of binding of ingredients, the modulation of cell cycle activity,

and detection of cell cycle regulation is not an adequate description of the claimed invention. For instance, nowhere in the present specification does Applicant disclose a description for the experimentation of combining the disclosed R0101 alleged alleged cell cycle protein with a candidate bioactive agent, and determining whether binding between the two ingredients has occurred. Nowhere in the present specification does Applicant provide a teaching as to how one of either ordinary skill in the art or those skilled artisan would determine whether binding has occurred, since Applicant has not adequately defined or given an example of a binding event. The Office recognizes Hitoshi declares that Applicants have isolated a nucleic acid that encodes R0101 protein (*i.e.,* SEQ ID NO:1) and provide both the nucleic acid and the encoded amino acid (*i.e.,* SEQ ID NO:2), however, even in view of the illustrated figures, it is unclear as how one would properly interpret the subject matter Applicant intends to direct the invention since Applicant provides no explanation of the experiments that have been performed. Thus, it is uncertain as to what the cited Figures purport to show.

Thus, Claims 15-17 and 20-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The broad generic claim lacks sufficient description to inform a skilled artisan that Applicant was in possession of the claimed invention at the time of filing since the specification lacks a sufficient number of species which have been described by complete structure or

identifying characteristics, thus the description requirement has not been satisfied, see Eli Lilly, 119 F. 3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1977).

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-17 and 20-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites the limitation "the cell" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 15 recites the limitation "the binding of said candidate bioactive agent" in line 5. There is insufficient antecedent basis for this limitation in the claim.

Claim 17 recites the limitation "said cell" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim 20 recites the limitation "the activity" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 20 recites the limitation "said R010 protein" in line 2. The claim lacks clear antecedent basis for this limitation. Applicant may overcome the rejection by replacing " R0101 protein" with alleged cell cycle protein R0101.

All other cited claims depend directly or indirectly from rejected claims and are, therefore, also, rejected under U.S.C. 112, second paragraph for the reasons set forth above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is (703) 308-9432. The examiner can normally be reached on Monday through Friday from 7:15 am to 3:45 pm. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196 or the Supervisory Patent Examiner, Brenda Brumback whose telephone number is (703) 306-3220.

MCF

October 1, 2003

Michele C. Flood

MICHELE C. FLOOD
PATENT EXAMINER